

Claims

1. A method of diagnosing a patient as having a neoplasia, said method comprising detecting an endocan nucleic acid molecule or polypeptide in a patient sample, wherein detection of an endocan nucleic acid or polypeptide indicates that said patient has a neoplasia.
2. The method of claim 1, wherein said patient sample is a blood sample.
3. The method of claim 1, wherein said patient sample is a tissue sample.
4. The method of claim 1, wherein said method comprises detecting an increase in the level of expression of an endocan polypeptide in a patient sample relative to the level of endocan polypeptide present in a corresponding control sample from a normal individual.
5. The method of claim 4, wherein said level of expression is determined in an immunological assay.
6. The method of claim 5, wherein said level of expression is detected by ELISA.
7. The method of claim 1, wherein said patient is asymptomatic.

8. A method of assessing the responsiveness of a neoplasm to a treatment regimen, said method comprising determining the level of an endocan nucleic acid or polypeptide in a patient sample relative to the level in a reference sample, wherein an alteration in said nucleic acid or polypeptide level in said patient sample indicates the responsiveness of said neoplasm to a treatment regimen.

9. The method of claim 8, wherein said reference sample is derived from a healthy individual.

10. The method of claim 8, wherein said patient is being treated for a neoplasm.

11. The method of claim 8, wherein said reference sample is obtained from said patient prior to or during the course of said treatment regimen.

12. The method of claim 8, wherein said patient sample is a blood sample.

13. The method of claim 8, wherein said patient sample is a tissue sample.

14. The method of claim 8, wherein said alteration is an increase, and said increase indicates a decreased responsiveness of said neoplasm to a treatment regimen.

15. The method of claim 8, wherein said alteration is a decrease, and said decrease indicates an increased responsiveness of said neoplasm to a treatment regimen.

16. The method of claim 8, wherein said neoplasm is a renal cell carcinoma, a lung cancer, a glioma, or a breast carcinoma.
17. A method of determining the prognosis of a patient having a neoplasm, said method comprising detecting an alteration in the level of an endocan nucleic acid molecule or polypeptide in a patient sample relative to the level in a reference sample, wherein an alteration indicates the prognosis of said patient.
18. The method of claim 17, wherein said reference sample is obtained from said patient prior to or during the course of said treatment regimen.
19. The method of claim 17, wherein said alteration is an increase, and said increase indicates a poor prognosis.
20. The method of claim 17, wherein said alteration is a decrease, and said decrease indicates a good prognosis.
21. The method of claim 17, wherein said patient sample is a tissue sample or a blood sample.
22. The method of claim 17, wherein said level of expression is determined in an immunological or enzymatic assay.
23. The method of claim 17, wherein said neoplasm is a renal cell carcinoma, a lung cancer, a glioma, or a breast carcinoma.

24. A diagnostic kit for the detection of a neoplasm in a patient comprising an endocan nucleic acid or amino acid sequence, or a fragment thereof.

25. A diagnostic kit for the detection of a neoplasm in a patient comprising an anti-endocan antibody.

26. A method of treating or preventing a neoplasm, said method comprising administering to a patient in need of such treatment an effective amount of a pharmaceutical composition comprising an inhibitory endocan nucleic acid molecule with complementarity to an endocan nucleic acid molecule or fragments thereof.

27. The method of claim 26, wherein said nucleic acid molecule is an antisense nucleic acid molecule that decreases the expression of an endocan nucleic acid molecule or polypeptide in a cell.

28. The method of claim 26, wherein said inhibitory endocan nucleic acid molecule is an double stranded nucleic acid molecule, siRNA, or shRNA that decreases the expression of an endocan nucleic acid molecule or polypeptide.

29. A method of treating or preventing a neoplasm, said method comprising administering to a patient in need of such treatment an effective amount of a pharmaceutical composition comprising an inhibitor of endocan biological activity.

30. The method of claim 29, wherein said inhibitor is an antibody or an antigen-binding fragment thereof that specifically binds endocan.

31. The method of claim 29, wherein said antibody is a monoclonal antibody.
32. The method of claim 29, wherein said antibody or antigen-binding fragment thereof is a human or humanized antibody.
33. The method of claim 29, wherein said antibody lacks an Fc portion.
34. The method of claim 29, wherein said antibody is an F(ab')₂, and Fab, or an Fv structure.
35. The method of claim 29, wherein said antibody or antigen-binding fragment thereof is present in a pharmaceutically acceptable carrier.
36. The method of claim 29, wherein said inhibitor is an inhibitor of a protein kinase C signaling pathway.
37. The method of claim 36, wherein said inhibitor is bisindolylmaleimide I, ruboxistaurin, or CGP41251.
38. The method of claim 29, wherein said inhibitor is an anti-VEGF antibody.
39. The method of claim 29, wherein said inhibitor is an Flk-1 antagonist.
40. The method of claim 39, wherein said antagonist is SU1498.
41. The method of claim 26 or 29, wherein said neoplasm is a renal cell carcinoma, a lung cancer, a glioma, or a breast carcinoma.

42. A method of identifying a candidate compound that may inhibit a neoplasm, said method comprising contacting a cell that expresses an endocan nucleic acid molecule with a candidate compound, and comparing the level of said nucleic acid molecule in said cell contacted by said candidate compound with the level of said nucleic acid in a control cell not contacted by said candidate compound, wherein a decrease in the level of said endocan nucleic acid molecule identifies said candidate compound as a candidate compound that may inhibit a neoplasm.

43. The method of claim 42, wherein said decrease in expression is a decrease in transcription.

44. The method of claim 43, wherein said decrease in expression is a decrease in translation.

45. The method of claim 42, wherein said cell is *in vivo*.

46. The method of claim 42, wherein said cell is *in vitro*.

47. The method of claim 42, wherein said cell is a human umbilical vein endothelial cell.

48. The method of claim 42, wherein said cell is grown in the presence of a tumor derived factor.

49. A method of identifying a candidate compound that inhibits a neoplasm, said method comprising contacting a cell that expresses an endocan polypeptide with a candidate compound, and comparing the level of endocan polypeptide in said cell contacted by said candidate compound with the level of endocan polypeptide in a control cell not contacted by said candidate compound, wherein a decrease in the level of endocan polypeptide identifies said candidate compound as a candidate compound that inhibits a neoplasm.

50. The method of claim 49, wherein said decrease in expression is assayed using an immunological assay, an enzymatic assay, or a radioimmunoassay.

51. The method of claim 49, wherein said cell is a human umbilical vein endothelial cell.

52. The method of claim 49, wherein said cell is grown in the presence of a tumor derived factor.

53. The method of claim 49, wherein said tumor-derived factor is present in conditioned culture media.

54. A method of identifying a candidate compound that inhibits a neoplasm, said method comprising contacting a cell that expresses endocan with a candidate compound, and comparing endocan biological activity in said cell contacted by said candidate compound with the level of endocan biological activity in a control cell not contacted by said candidate compound, wherein a decrease in the level of endocan biological activity identifies said candidate compound as a candidate compound that inhibits a neoplasm.

55. The method of claim 54, wherein said cell is a neoplastic cell.

56. The method of claim 54, wherein endocan biological activity is assayed by measuring the viability or proliferation of said cell.

57. The method of claim 54, wherein said cell is an endothelial cell.

58. The method of claim 57, wherein said endothelial cell is a neoplasm endothelial cell.

59. The method of claim 57, wherein said endocan biological activity is assayed by measuring tumor size, cell number, or viability.

60. The method of claim 57, wherein said cell is grown in the presence of a tumor-derived factor.*

61. The method of claim 59, wherein said tumor-derived factor is present in conditioned culture media.

62. The method of claim 59, wherein said endocan biological activity is promotion of angiogenesis.

63. A pharmaceutical composition comprising an isolated endocan inhibitory nucleic acid molecule, or portion thereof, formulated in a pharmaceutically acceptable carrier.

64. The method of claim 63, wherein said nucleic acid molecule is a double stranded nucleic acid molecule with complementarity to an endocan nucleic acid molecule that decreases expression of an endocan nucleic acid molecule or polypeptide in a cell.

65. The method of claim 63, wherein said nucleic acid molecule is an antisense nucleic acid molecule that with complementarity to an endocan nucleic acid molecule decreases the expression of an endocan nucleic acid molecule or polypeptide in a cell.

66. A method of identifying a neoplasm endothelium-specific promoter, said method comprising:

- (a) providing an expression construct comprising at least a tumor-factor responsive nucleic acid sequence and a minimal core promoter operably -linked to a nucleic acid sequence that encodes a protein;
- (b) transforming a cell with said construct; and
- (c) detecting expression of said construct in said cell, wherein a promoter that directs expression in said cell is a neoplasm endothelium-specific promoter.

67. The method of claim 66, further comprising the steps of

- (d) providing an Hprt targeting vector comprising said endothelium-specific promoter;
- (e) transforming a mouse with said vector;
- (f) detecting expression of said vector in neoplasm endothelium.

68. The method of claim 66, wherein said minimal core promoter comprises a portion of a Tie-2 promoter.

69. The method of claim 66, wherein said encoded protein is a detectable reporter.

70. The method of claim 68, wherein said tumor-factor responsive nucleic acid sequence is selected from the group consisting of tumor-responsive elements of an endocan promoter, tumor-responsive elements in promoters of transgenes that direct expression during tumor angiogenesis, and hypoxia response elements.

71. A method of delivering a polypeptide to a neoplasm, said method comprising:

- (a) providing a construct comprising the promoter of claim 66; and
- (b) transforming a cell with said construct patient under conditions suitable for expressing said nucleic acid in said construct, whereby said construct expresses said product in said tumor.

72. A neoplasm endothelium-specific promoter comprising at least a tumor-factor responsive nucleic acid sequence and a minimal core promoter, wherein said promoter when operably linked to a heterologous nucleic acid molecule directs expression of said nucleic acid molecule in a tumor endothelial cell.

73. The promoter of claim 72, wherein said promoter comprises at least a portion of an endocan or Flt-1 nucleic acid molecule.

74. An expression construct comprising the promoter of claim 72, wherein said promoter is positioned for expression.

75. A transformed cell expressing the construct of claim 74.